REMARKS

Claim 1 is deleted without prejudice or disclaimer, and claims 2-4, 10-12, and 23 are amended, to facilitate prosecution and allowance of the now pending claims. Applicants hereby reserve the right to file continuing applications or take any other such appropriate measure to prosecute the invention of the cancelled subject matter.

Claims 2-4, 10-12, and 23 –25 are now pending in the application.

A marked-up version of the changes made to the specification are found in the "Version with markings to show changes made" attached to this paper.

Specification

Page 9, lines 35-38, of the specification was objected to because of the following informality: recitation of the term "SEQ ID N°". This objection is obviated by appropriate correction as set forth above.

Withdrawal of the rejections under 35 U.S.C §112, first paragraph, is respectfully requested

Claims 1 and 12 stand rejected under 35 U.S.C §112, first paragraph, the Office Action indicating that the specification, while enabling for nucleotides encoding SEQ ID NO: 20 and 22, does not reasonably provide enablement for a nucleic acid encoding any other polypeptide.

With regard to Claims 1 and 12, this rejection is respectfully traversed for reasons of record. Nevertheless, to facilitate prosecution and allowance of the now pending claims, claim 1 is deleted and claim12 is amended. Claim 12 is now made dependent on claim 2 which includes a limitation drawn to a nucleic acid encoding a secreted soluble calcium channel subunit polypeptide that binds gabapentin, and comprises a polynucleotide having at least 90% identity with the sequence encoding:

- from amino-acid 1 to between amino-acids 1027 and 1062 of SEQ ID N°20 or
- from amino-acid 1 to between amino-acids 984 and 1019 of SEQ ID N°22.

Thus, claim 2 sets forth the specific limitations drawn to a secreted soluble polypeptide, that binds gabapentin, as well as specific sequence limitations. Support for these amendments can be found throughout the specification and the original claims. See, for example, specification page 8, line 10 to page 9, line 19; and page 20, lines 14-26. Accordingly, guidance is provided as to the specific range of amino acids within the sequences of SEQ ID NO:20 and 22 that can be utilized by the ordinarily skilled artisan in making the claimed nucleic acids under consideration. Furthermore, the specification teaches modification of the polypeptides encoded by the nucleotides of the invention by equivalent amino acid substitution, and/or tagging. See for example, page 20, final paragraph to page 21, and page 13, lines 21-30. Furthermore, the specification teaches how to test for gabapentin binding and provides specific examples of the secreted soluble polypeptides encompassed by claim 2 that bind gabapentin. See, for example, specification Examples 6-8 and Office Action, page 4, paragraph (7).

Applicants respectfully submit that it is well settled law that extensive experimentation is not undue experimentation; and that working examples of every permutation of the invention are not required for an enabling disclosure. Thus, Applicants submit that with the guidance provided in the specification, it would be well within the skill of the ordinarily skilled artisan to make the claimed polypeptides under consideration and test whether they are a secreted soluble polypeptide, and whether they bind gabapentin. Thus, Applicants respectfully submit that the specification fully enables the ordinarily skilled artisan, to make and use the invention commensurate in scope with claim 2.

In view of the above, withdrawal of the rejection of Claims 1 and 12 under 35 USC §112, first paragraph is respectfully requested.

Claims 2-3 and 23 stand rejected under 35 U.S.C §112, first paragraph, the Office Action indicating that the specification while being enabling for a polynucleotide encoding a substantially purified polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 20 and 22, does not reasonably provide enablement for a polynucleotide encoding

a substantially purified variant having at least 90% amino acids sequence identity to SEQ ID NO 20 and 22. Thus, the Office Action indicates that specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected to make and use the invention commensurate in scope with these claims.

As more fully explained above, claim 2 is amended to set forth the specific limitations drawn to a secreted soluble polypeptide, that binds gabapentin, as well as specific sequence limitations. Also as more fully explained above, Applicants submit that present claim 2 is fully enabled by the specification. It is noted that claim 2 is amended to exclude the limitation drawn to equivalent amino acid substitutions. This subject matter is presented independently in new claim 24 as more fully explained below.

With respect to claim 3, claim 3 is amended to also include limitations drawn to a secreted soluble polypeptide, that binds gabapentin, as well as specific sequence limitations. Applicants submit that the above statements made in support of amendment and enablement of claim 2 are also applicable to claim 3. Furthermore, claim 3 is amended to emphasize a closed claim structure by including a limitation drawn to a sequence that is at least 90% identical with the sequences encoding particular amino acid sequences of SEQ ID NO's 20 and 22.

With respect to claim 23, claim 23 is amended to also include limitations drawn to a secreted soluble polypeptide, that binds gabapentin, as well as specific sequence limitations. Furthermore, the claim is amended to emphasize a closed claim structure by including a limitation drawn to a sequence that is at least 90% identical with the sequences encoding the amino acid sequences set forth in SEQ ID NO:'s 1, 2, 3, 7, 8, 9, 13, 14, and 15.

In view of amended Claims 2, 3, and 23; withdrawal of the rejection of those claims under 35 USC §112, first paragraph is respectfully requested.

Withdrawal of the rejecti ns under 35 U.S.C §112, second paragraph, is respectfully requested

Claims 1-4, and 10-12 stand rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Office Action indicates that this rejection of claims 1 and 12 was based on recitation of an arbitrary protein name without any structural limitations. As more fully explained above, claim 1 is cancelled and claim 12 is made dependent on claim 2. Claim 2 is amended as more fully explained above to contain limitations drawn to a nucleic acid encoding a secreted soluble calcium channel subunit polypeptide that binds gabapentin, and comprises a polynucleotide having at least 90% identity with the sequence encoding:

- from amino-acid 1 to between amino-acids 1027 and 1062 of SEQ ID N°20 or
- from amino-acid 1 to between amino-acids 984 and 1019 of SEQ ID N°22.

Applicants submit that in view of these amendments, which include the structural limitations placed in claim 2, this rejection of claims 1 and 12 is obviated and should be withdrawn.

Claims 2-3 stand rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Office Action indicates that this rejection of claims 2-3 was based on recitation of the terms "equivalent", "specificity", and "affinity". To facilitate prosecution, claims 2 and 3 are amended to exclude the recitation of these terms. Accordingly, this rejection of claims 1 and 12 is obviated and should be withdrawn.

As noted above, the subject matter of claim 2 drawn to equivalent amino acids is now presented in better form as independent claim 24. Applicants respectfully submit that in light of the teaching provided in the specification, the term "equivalent" is adequately defined to apprise one of ordinary skill in the art of the metes and bounds of the invention. See, for example, specification page 20, line 28, to page 21. Accordingly, Applicants submit that this rejection of the claims should not be extended to new claim 24.

Withdrawal f the rejections under 35 U.S.C §102(b) is respectfully requested

Claims 1, 4, 10-12 and 23 stand rejected under 35 USC §102(b) based on anticipation by Wei et al. (1998) reference of record.

As more fully explained above, claim 1 is deleted, and claims 10-12 are now made dependent on claim 2. Accordingly, this rejection of claims 1 and 10-12 is obviated. Regarding this rejection of claims 4 and 23, the Office Action further indicates that despite the Applicants' arguments presented in the response submitted October 5, 2001, the reason for maintaining this rejection of claims 4 and 23, is that "claims 4 and 23 use open language to describe the nucleic acid sequence." This rejection is respectfully traversed.

In pertinent part, and prior to this response, claim 4 sets forth "...wherein said sequence is the sequence of SEQ ID N°1, SEQ ID N°2, SEQ ID N°3, SEQ ID N°7, SEQ ID N°8, SEQ ID N°9, SEQ ID N°13, SEQ ID N°14, or SEQ ID N°15" (emphasis added). Thus, in contrast to the Office Action, Applicants submit that claim 4, though previously dependent on claim 1, contained closed language to describe the nucleic acid sequence. Accordingly, Applicants respectfully submit that maintaining this rejection of claim 4 is not proper. It is noted that claim 4 is now made independent, without affecting this closed language.

To facilitate prosecution, claim 23 is amended to emphasize the closed language description of the nucleic acid sequences. This amendment is set forth in the marked up copy of the claims submitted herewith as follows: "A purified or isolated nucleic acid [having] <u>encoding a secreted soluble calcium channel subunit polypeptide that binds gabapentin, wherein the nucleotide sequence of said nucleic acid is</u> at least 90% [identity] <u>identical</u> with the nucleotide sequence of SEQ ID....". Accordingly, as the Examiner appears to interpret the term "having" as open-ended, this rejection of claim 23 is obviated by amendment.

Claims 1, 10-12 and 23 stand rejected under 35 USC §102(b) based on anticipation by the Harpold et al. reference of record (WO 9504822). The Office Action indicates that this rejection of claims 1 and 10-12 is based on Harpold et al's disclosure of a "human voltage gated calcium channel subunit", and subsequent cloning into an expression vector, transfection, and protein isolation.

As more fully explained above, claim 1 is deleted, and claims 10-12 are now made dependent on claim 2. Accordingly, this rejection of claims 1 and 10-12 is obviated.

With respect to this rejection of claim 23, the office action indicates that the rejection is maintained because claim 23 uses open language. As more fully explained above, claim 23 is amended to emphasize the closed language description of the nucleic acid sequences. This amendment is set forth in the marked up copy of the claims submitted herewith as follows: "A purified or isolated nucleic acid [having] encoding a secreted soluble calcium channel subunit polypeptide that binds gabapentin, wherein the nucleotide sequence of said nucleic acid is at least 90% [identity] identical with the nucleotide sequence of SEQ ID....". Accordingly, as the Examiner appears to interpret the term "having" as open-ended, this rejection of claim 23 is obviated by amendment.
In view of the arguments set forth above withdrawal of the rejection of Claims 1, 10-12, and 23 under 35 USC §102(b) is respectfully requested.

New claim 25 is added. New claim 25 is supported throughout the specification and original claims. For example, see specification page13, lines 21-30. In view of the above, Applicants submit that new claim 25 is free of the aforementioned rejections.

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is earnestly solicited.

The Commissioner is hereby authorized to charge any fees under 37.C.F.R §1.116 and 1.117 that may be required by this paper to Deposit Account No. 23-0455.

In the event the Examiner wishes to discuss any matter concerning this application, he is invited to communicate with the undersigned.

Respectfully submitted,

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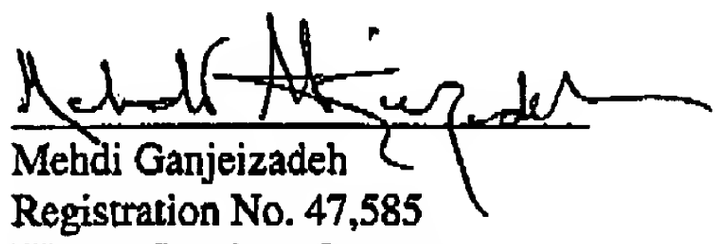

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Attachment - Amendments to the specification and claims, Version with markings to show changes made

"Version with markings to show changes made."

IN THE SPECIFICATION:

At page 9, lines 35-38:

In a first preferred embodiment of the above method, the nucleic acid encodes a secreted soluble $\alpha_2\delta$-2, $\alpha_2\delta$-3 or $\alpha_2\delta$-4 subunit polypeptide of [SEQ ID N°4, SEQ ID N°5, SEQ ID N°6, SEQ ID N°10, SEQ ID N°11, SEQ ID N°12, SEQ ID N°16, SEQ ID N°17 and SEQ ID n°18] SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 16, SEQ ID NO: 17 and SEQ ID NO: 18.

IN THE CLAIMS:

Claim 1 is deleted.

Claims 2, 3, 4, 10, 11, and 23 are amended as follows:

Claim 2 (Twice amended). A purified or isolated nucleic acid [according to claim 1,] encoding a secreted soluble calcium channel subunit polypeptide that binds gabapentin said nucleic acid comprising a polynucleotide having at least 90% identity with the sequence encoding:

- from amino-acid 1 to between amino-acids 1027 and 1062 of SEQ ID N°20 [for $\alpha_2\delta$-2], or

- from amino-acid 1 to between amino-acids 984 and 1019 of SEQ ID N°22 [for $\alpha_2\delta$-3 wherein the differing nucleotides encode amino acids which are the same as the amino acids of the SEQ ID N°20 and SEQ ID N°22 through codon degeneracy or encode amino acids which are equivalent to the amino acids of SEQ ID N°20 and SEQ ID N°22 either by structural homology, by net charge or hydrophobicity similarity, such that the encoded polypeptide retains its specificity and affinity properties to the biological targets of the parent polypeptides].

Claim 3 (Twice amended). A purified or isolated nucleic acid [according to claim 1,] encoding a secreted soluble calcium channel subunit polypeptide that binds gabapentin [having], wherein the sequence of said nucleic acid is at least 90% [identity] identical with the sequence encoding:

- from amino-acid 1 to between amino-acids 1047 and 1062 of SEQ ID N°20 [for $\alpha_2\delta$-2], or

- from amino-acid 1 to between amino-acids 1004 and 1019 of SEQ ID N°22 [for $\alpha_2\delta$-3 wherein the differing nucleotides encode amino acids which are the same as the amino acids of the SEQ ID N°20 and SEQ ID N°22 through codon degeneracy or encode amino acids which are equivalent to the amino acids of SEQ ID N°20 and SEQ ID N°22 either by structural homology, by net charge or hydrophobicity similarity, such that the encoded polypeptide retains its specificity and affinity properties to the biological targets of the parent polypeptides].

Claim 4 (Twice amended). A purified or isolated nucleotide sequence [according to claim 1,] encoding a secreted soluble calcium channel subunit polypeptide wherein said sequence is the sequence of SEQ ID N°1, SEQ ID N°2, SEQ ID N°3, SEQ ID N°7, SEQ ID N°8, SEQ ID N°9, SEQ ID N°13, SEQ ID N°14, or SEQ ID N°15.

Claim 10 (Amended). A recombinant vector comprising a nucleic acid according to claim [1] 2.

Claim 11 (Amended). A recombinant host cell comprising a nucleic acid according to claim [1] 2.

Claim 12 (Amended). A method for producing a secreted soluble [$\alpha_2\delta$-n subunit wherein n is 2, 3 or 4, and] calcium channel subunit polypeptide, said method comprises the steps of:

(a) inserting the nucleic acid according to claim 2 [encoding the desired $\alpha_2\delta$-n subunit polypeptide] in an appropriate vector;

(b) culturing, in an appropriate culture medium, a host cell previously transformed or transfected with the recombinant vector of step (a);

(c) harvesting the culture medium thus obtained or lyse the host cell, for example by sonication or osmotic shock;

(d) separating or purifying, from said culture medium, or from the pellet of the resultant host cell lysate, the thus produced [$\alpha_2\delta$-n] calcium channel subunit polypeptide of interest.

Claim 23 (Amended). A purified or isolated nucleic acid [having] encoding a secreted soluble calcium channel subunit polypeptide that binds gabapentin, wherein the nucleotide sequence of said nucleic acid is at least 90% [identity] identical with the nucleotide sequence of SEQ ID N°1, SEQ ID N°2, SEQ ID N°3, SEQ ID N°7, SEQ ID N°8, SEQ ID N°9, SEQ ID N°13, SEQ ID N°14, or SEQ ID N°15.

New Claims 24 and 25 are added as follows:

Claim 24 (New). A purified or isolated nucleic acid encoding a secreted soluble calcium channel subunit polypeptide that binds gabapentin, said nucleic acid comprising a nucleotide sequence having at least 90% identity with the sequence encoding

- a polypeptide from amino-acid 1 to between amino-acids 1027 and 1062 of SEQ ID N°20 wherein said polypeptide that has one or several equivalent amino acid substitutions[for $\alpha_2\delta$-2], or

- a polypeptide from amino-acid 1 to between amino-acids 984 and 1019 of SEQ ID N°22 wherein said polypeptide has one or several equivalent amino acid substitutions.

Claim 25 (New). The nucleic acid of claim 2 further comprising a nucleotide sequence encoding a tag.